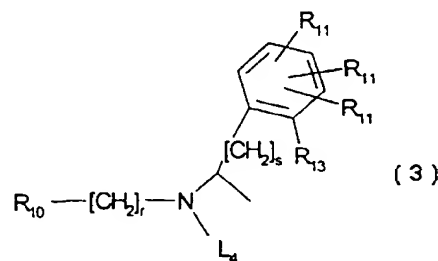
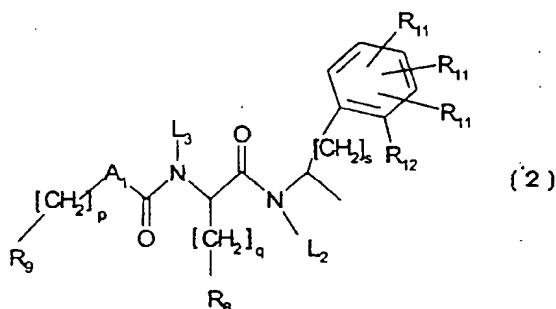
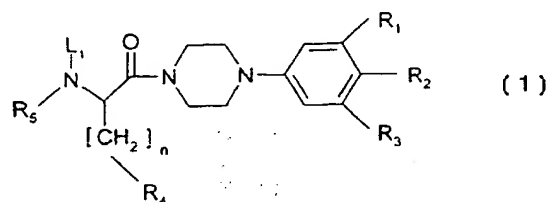




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : C07K 5/08, C07D 295/185, 209/20, A61K 38/06, 31/495, 31/496, C07D 405/12, 409/12, 401/12, 417/12		A1	(11) International Publication Number: WO 00/15657 (43) International Publication Date: 23 March 2000 (23.03.00)
(21) International Application Number: PCT/GB99/02957 (22) International Filing Date: 7 September 1999 (07.09.99) (30) Priority Data: 9819860.9 12 September 1998 (12.09.98) GB (71) Applicant (for all designated States except US): ZENECA LIMITED [GB/GB]; 15 Stanhope Gate, London W1Y 6LN (GB). (72) Inventors; and (75) Inventors/Applicants (for US only): LUKE, Richard, William, Arthur [GB/GB]; Alderley Park, Macclesfield, Cheshire SK10 4TG (GB). JEWSBURY, Philip, John [GB/GB]; Alderley Park, Macclesfield, Cheshire SK10 4TG (GB). COTTON, Ronald [GB/GB]; Alderley Park, Macclesfield, Cheshire SK10 4TG (GB). (74) Agent: BRYANT, Tracey; AstraZeneca PLC, Global Intellectual Property, Alderley Park, Mereside, Macclesfield, Cheshire SK10 4TG (GB).			(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>

(54) Title: PIPERIZINE-4-PHENYL DERIVATIVES AS INHIBITORS OF THE INTERACTION BETWEEN MDM2 AND 53



(57) Abstract

A compound of formula (1), wherein: R_5 is hydrogen, C_{1-4} alkyl, R_6CH_2- or $R_6C(O)-$; R_6 is aryl, heteroaryl, heterocyclyl, amino C_{3-6} alkyl, $N-(C_{1-4}$ alkyl)amino C_{3-6} alkyl, $NN-(diC_{1-4}$ alkyl)amino C_{3-6} alkyl, or R_7 ; wherein the aryl, heteroaryl or heterocyclyl rings may be optionally substituted with up to three substituents independently selected from nitro, C_{1-4} alkyl, C_{1-4} alkoxy, halo, $(C_{1-4}$ alkyl)sulfonyl, C_{1-4} alkoxycarbonyl, $N-(C_{1-4}$ alkyl)carbamoyl, $NN-(diC_{1-4}$ alkyl)carbamoyl, $N-(C_{1-4}$ alkyl)amino or $NN-(diC_{1-4}$ alkyl)amino; wherein R_7 is either a group or formula (2) or formula (3); and wherein $L_1, L_2, L_3, L_4, R_1, R_2, R_3, R_4, R_8, R_9, R_{10}, R_{11}, R_{12}, R_{13}, A, n, p, q, r$ and s are as defined in claim 1. The compounds of formula (1) inhibit the interactions between MDM2 and p53 and may be useful in the treatment of cancers.